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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| EXAMINER | |
|---|---|
| HARRIS, ALANA M | |
| **ART UNIT** | **PAPER NUMBER** |
| 1643 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|---|---|---|
| 31 DAYS | 02/23/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/782,968 | WILLIAMS, KEVIN J. | |
| | Examiner | Art Unit | |
| | Alana M. Harris, Ph.D. | 1643 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-240* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-240* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

***Election/Restrictions***

1. Applicant is put on notice that each thrombospondin fragment is regarded as an independent and distinct product. Consequently, each is subject to a separate Invention/Group. One Invention/Group is based upon one of the thirty-seven thrombospondin fragments.

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

1-37. Claims 1-20, 94-97, 150-152, 154-156, 158, 159, 165-174 and 225-227 and 235, drawn to a purified thrombospondin fragment identified as SEQ ID NO: 1-37, respectively, classified in class 530, subclass 300.

38-74. Claims 21-53, 80, 90, 93, 98-109, 160, 161, 175-179 and 195-215, drawn to a method to detect and/or quantify a thrombospondin fragment identified as SEQ ID NO: 1-37, respectively, classified in class 436, subclass 501.

75-111. Claims 54-59, 145-149, 153, 216 and 234, drawn to a method of producing antibodies against a thrombospondin fragment identified as SEQ ID NO: 1-37, respectively, classified in class 435, subclass 70.21.

112-148. Claims 60-63, 90, 163, 164, 217, 234 and 236, drawn to a method of producing a peptide or non-peptide binding agent against a thrombospondin fragment identified as SEQ ID NO: 1-37, respectively, classified in class 435, subclass 89.

149-185. Claims 64, 65 and 218, drawn to a cell line capable of producing a binding agent against a thrombospondin fragment identified as SEQ ID NO: 1-37, respectively, classified in class 436, subclass 548. OR classified in class 435, subclass 325.

186-222. Claims 66-79, 81-89, 157 and 219-224, drawn to a kit for the determination of the presence of, and/or the amount of, and/or the concentration of, a thrombospondin fragment identified as SEQ ID NO: 1-37, respectively, classified in class 436, subclass 86.

223-259. Claims 110-144, 162 and 228-233, drawn to a method to detect the presence and/or clinical course of a neoplastic disease comprising measuring the plasma level of a thrombospondin fragment identified as SEQ ID NO: 1-37, respectively, classified in class 436, subclass 8.

260-296. Claims 180-185, drawn to a method of distinguishing between a cancerous sample of bodily fluid and a non-cancerous sample of bodily fluid comprising implementing a binding agent and detecting thrombospondin, classified in class 435, subclass 7.1.

297-333. Claims 186-194, drawn to method of distinguishing between properly and improperly collected plasma samples comprising implementing a binding agent and detecting the presence of thrombospondin, classified in class 436, subclass 512.

334. Claims 237 and 238, drawn to a method that distinguishes two thrombospondin fragments from each other comprising implementing a

binding agent to obtain a quantitation and utilizing the difference between the quantitations in the amounts of first and second fragments, classified in class 435, subclass 4.

335. Claims 239 and 240, drawn to an aptamer, classified in class 536, subclass 18.7.

3. This application contains claims directed to the following patentably distinct species:

a. glycosylation,

b. deglycosylation,

c. β-hydroxylation,

d. alkylation,

e. reduction,

f. denaturation,

g. renaturation,

h. calcium depletion,

i. calcium supplementation,

j. conjugation, and

k. addition of groups or moieties. The species listed in claims 5, 164 and 235 are independent or distinct because each process involves distinct methods of the transfer, removal or addition of one molecule to another, as well as the alteration of molecules.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1-4, 6-20, 60, 61, 63, 94-97, 151, 152, 154-156, 158, 159, 163, 165-171, 173, 174, 217, 225-227, 234 and 236 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

4. This application contains claims directed to the following patentably distinct species:

a. cancer,

b. renal disease (including renal failure),

c. atopic dermatitis,

d. vasculitis (including acute vasculitis, non-specific vasculitis, vasculitis syndrome),

e. renal allograft,

f. asthma,

g. diabetes mellitus,

h. myocardial infarction,

i. liver disease,

j. splenectomy,

k. dermatomyositis,

l. polyarteritis nodosa,

m. lupus erythematosus (including systemic lupus erythematosus),

n. Kawasaki syndrome,

o. rheumatoid arthritis (including juvenile rheumatoid arthritis),

p. purpura (including Henoch-Schonlein purpura, thrombocytopenic purpura),

q. an inflammatory condition,

r. a condition associated with clotting,

s. a condition associated with platelet activation (including a condition associated with intravascular platelet activation, a condition associated with consumption if platelets),

t. heparin-induced thrombocytopenia,

u. disseminated intravascular coagulation, intravascular coagulation,

v. extravascular coagulation,

w. a condition associated with endothelial activation,

x. a condition associated with production and/or release of thrombospondin and/or a thrombospondin fragment,

y. urticaria,

z. hives,

aa. angioedema,

bb. a drug reaction,

cc. an antibiotic reaction,

dd. an aspartame reaction,

ee. eczema (including atopic dermatitis),

ff. hypersensitivity,

gg. scleroderma,

hh. conditions associated with plugging of vessels,

ii. a condition associated with a cryofibrinogen,

jj. a condition associated with a cryoglobulin, and

kk. a condition associated with an anti-cardiolipin antibody. The species listed in claims 34 and 204, are independent or distinct because each disorder and disease differs in histopathobiology, which cause different types of discomfort, dysfunction, and/or distress. If Applicants elect cancer they must further select a distinct cancer as listed in section 4.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is

finally held to be allowable. Currently, 21-33, 35-42, 44, 47, 49-53, 53, 80, 90, 93, 98-107, 160, 161, 175-179, 195-203, 205, 207-211, 214 and 215 generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

5. This application contains claims directed to the following patentably distinct species:

a. adenoma,

b. adenocarcinoma,

c. carcinoma,

d. lymphoma,

e. leukemia,

f. solid cancer,

g. liquid cancer,

h. metastatic cancer,

i. pre-metastatic cancer,

j. non-metastatic cancer,

k. a cancer with vascular invasion,

l. internal cancer,

m. skin cancer,

n. cancer of the respiratory system,

o. cancer of the circulatory system,

p. cancer of the musculoskeletal system,

q. cancer of a muscle,

r. cancer of a bone,

s. cancer of a joint,

t. cancer of a tendon or ligament,

u. cancer of the digestive system,

v. cancer of the liver or biliary system,

w. cancer of the pancreas,

x. cancer of the head,

y. cancer of the neck,

z. cancer of the endocrine system,

aa. cancer of the reproductive system,

bb. cancer of the male reproductive system,

cc. cancer of the female reproductive system,

dd. cancer of the genitourinary system,

ee. cancer of a kidney,

ff. cancer of the urinary tract,

gg. cancer of a sensory system,

hh. cancer of the nervous system,

ii. cancer of a lymphoid organ,

jj. blood cancer,

kk. cancer of a gland,

ll. cancer of a mammary gland,

mm. cancer of a prostate gland,

nn. cancer of an endometrial tissue,

oo. cancer of a mesodermal tissue,

pp. cancer of an ectodermal tissue,

qq. cancer of an endodermal tissue,

rr. a teratoma,

ss. a poorly-differentiated cancer,

tt. a well-differentiated cancer, and

uu. a moderately differentiated cancer. The species listed in claims 36, 116, 118, 119 and 206 are independent or distinct because each cancer differs in histopathobiology, etiologic agents and treatment modalities.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is

finally held to be allowable. Currently, 21-32, 35, 37-53, 80, 90, 93, 98-117, 120-130, 133-144, 160, 161, 175-179, 195-204 and 212-214 generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

6. This application contains claims directed to the following patentably distinct species:

a. a platelet inhibitor,

b. a protease inhibitor,

c. a serine protease inhibitor,

d. an enzyme inhibitor,

e. an inhibitor of an enzyme that is divalent cation dependent,

f. a heparin (including a heparin fragment, a low-molecular weight heparin, a heparin sulfate),

g. an anticoagulant,

h. a COX inhibitor,

i. an inhibitor of a cell-adhesion molecule,

j. an inhibitor of a surface receptor,

k. a glycoprotein inhibitor, an inhibitor of a glycoprotein IIb/IIIa receptor,

l. a thrombin inhibitor,

m. an inhibitor of degranulation,

n. a chelator,

o. a citrate compound,

p. theophylline,

q. adenosine, and

r. dipyridamole. The species listed in claim 43 are independent or distinct because molecule differs in structure and method of implementing prevention or reduction of platelet activation and/or protease activity.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, 21-42, 44-53, 80, 90, 93, 98-109, 160, 161, 175-179, 195-204 and 212-214 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim

is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

7. This application contains claims directed to the following patentably distinct species:

a. an imaging test,

b. a radiographic test,

c. a nuclear medicine test,

d. magnetic resonance imaging test,

e. a blood test,

f. biopsy,

g. a histologic test,

h. a cytologic test,

i. an immunohistologic test,

j. a genetic test,

k. a guaiac test,

l. a test for a fecal cancer (including a test for fecal occult blood, a test for fecal blood, a test for fecal DNA, a test for a fecal cancer marker),

m. a cancer test not based on a thrombospondin fragment or portion thereof,

n. a receptor test,

o. an estrogen receptor test,

p. a disease test not based on a thrombospondin fragment or portion thereof,

m. an endoscopy (including an upper gastrointestinal endoscopy, a lower gastrointestinal endoscopy),

n. a colonoscopy,

o. a sigmoidoscopy,

p. a gastroscopy,

q. a laparoscopy,

r. a laparatomy,

s. a lymph node biopsy,

t. a surgery, and

u. a bronchoscopy. The species listed in claims 45, 48 and 212, are independent or distinct because the methods of assay are different in application, manner of examination and instruments used in performing particular exam. If Applicants elect a blood test they must further elect a particular blood test set forth in claim 46 in the following section.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, 21-33, 35-42, 44, 47, 49-53, 53, 80, 90, 93, 98-107, 160, 161, 175-179, 195-203, 205, 207-211, 214 and 215 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

8. This application contains claims directed to the following patentably distinct species:

a. thrombospondin receptor (including a thrombospondin binding protein, a thrombospondin receptor and/or binding protein that binds within a protease-resistant core region, a thrombospondin receptor and/or binding protein that binds a TSP fragment present in the plasma of a cancer patient),

b. a CSVTCG (SEQ ID NO:54) receptor (including a CSVTCG (SEQ ID NO:54) binding molecule),

c. an anti-secretory factor,

d. an angiocidin,

e. a 26S proteasome non-ATPase regulatory subunit 4,

f. a CD36, a fragment thereof, and

g. combinations. The species listed in claims 77 and 131 are independent or distinct because the molecules differ in structure and conformation. Elected species will be examined, as well as the fragment thereof, chimeras, and recombinant versions of said receptors and fragments. If Applicants elect species g. they must note the combination they would like examined and list the members of the combinations and note which member of the combination the novelty lies.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 21-33, 35-42, 44, 47, 49-53, 53, 80, 90, 93, 98-107, 110-117, 120-130, 133-144, 160-162, 175-179, 195-203, 205, 207-211, 214, 215 and 228-233 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

9. This application contains claims directed to the following patentably distinct species:

a. a cancer antigen test,

b. a cancer gene test (including a cancer DNA test),

c. a cancer RNA test (including a cancer mRNA test),

d. a cancer protein test, a

e. cancer glycoprotein test,

f. a cancer carbohydrate test,

g. a cancer lipid test,

h. a prostate specific antigen test,

i. a test of carcinoembryonic antigen,

j. a test of cancer antigen CA-125,

k. a test of alpha-fetoprotein,

l. a test of CA15-3,

m. a test of CA19-9,

n. a test of malignin,

o. a test of anti-malignin antibody,

p. a test of anti-secretory factor,

q. a cancer antigen that contains a carbohydrate epitope,

r. a cancer antigen that contains a protein or polypeptide epitope,

s. a cancer antigen that contains a lipid epitope,

t. a cancer antigen that contains a mixed epitope,

u. CA 27.29, and

v. episialin. The species listed in claims 46, 49 and 213 are independent or distinct because they are distinct and different laboratory tests/ medical tests done on blood to gain information of disease states and the function of organs. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 21-33, 35-42, 44, 47, 49-53, 53, 80, 90, 93, 98-107, 160, 161, 175-179, 195-203, 205, 207-211, 214 and 215 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after

the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

10. This application contains claims directed to the following patentably distinct species:

a. antibodies (a polyclonal antibody, a monoclonal antibody, a single-chain antibody),

b. a non-antibody,

c. a protein,

d. a product of phage display,

e. an aptamer,

f. a DNA (a modified DNA),

g. a RNA (a modified RNA),

h. a carbohydrate,

i. a glycosaminoglycan,

k. a heparin,

l. a glycoprotein,

m. a proteoglycan,

n. and combinations.

The species listed in claims 61, 62, 109, 131, 132, 144, 172 and 192 are independent or distinct because these molecules differ in structure, conformation and are made by materially distinct processes. The elected species will be examined, as

well as derivatives thereof. If Applicants elect species n. they must note the combination they would like examined and list the members of the combinations and note which member of the combination the novelty lies. If Applicants elect species e. they must indicate which one subsequence of nucleic acid or protein they want examined.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, 21-33, 35-42, 44, 47, 49-53, 53, 60, 61, 63, 80, 90, 93, 98-107, 110-117, 120-130, 133-144, 160-163, 175-179, 186-191, 193-203, 205, 207-211, 214, 215, 228-233 and 236 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

11. This application contains claims directed to the following patentably distinct species:

a. an integrin,

b. an RGD receptor,

c. an RFYVVMWK (SEQ ID NO:55) receptor,

d. an RFYVVM (SEQ ID NO:56) receptor,

e. an FYVVMWK (SEQ ID NO:57) receptor,

f. an IRVVM (SEQ ID NO:58) receptor,

g. a CSVTCG (SEQ ID NO:54) receptor and a CSVTCG (SEQ ID NO:54) binding molecule,

h. CD36,

i. anti-secretory factor,

j. angiocidin,

k. 26S proteasome non-ATPase regulatory subunit 4, and

l. combinations. The species listed in claims 88, 131 and 143 are independent or distinct because they differ in structure and conformation. Each listed binding agent differs in affinity and recognition ability. The elected species will be examined, as well as chimeras, and recombinant versions of said receptors, integrins, and fragments. If Applicants elect species l. they must note the combination they would like examined and list the members of the combinations and note which member of the combination the novelty lies.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 66-76, 78, 79, 81-87, 89, 110-117, 120-130, 133-142, 144, 157, 162, 219-224 and 228-233 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

12. If Applicant elects any one of Groups 112-148, 149-185, 186-222, 223-259, 260-296, 297-333 and 334 they *must further elect* the binding agent/species presented in claim 61.

13. Groups 1-37, 149-185, 186-222 and 335 are structurally and functionally different products, which are made by different methods and have different uses. The examination of all groups would require different searches in the U.S. Patent Shoes and

the scientific literature and would require the consideration of different patentability issues.

The products of Groups 1-37 are thrombospondin fragments, which each differs in structure and amino acid residues. The products of Groups 149-185 are cell lines, which are perpetuating strains of cells in laboratory culture, whereas the kits of 186-222 comprise components and reagents for a detection method. Aptamers of Invention 335 are any subsequence of nucleic acid or protein implemented in binding a specific target molecule.

Inventions 38-74, 75-111, 112-148 and 223-259 are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, although the different inventions read on in vitro methods they differ in the method objectives, method steps and parameters and in the reagents used. For example, the methods of Inventions 75-11 requires the manipulation of the cells to produce antibodies, whereas the method of Inventions 223-259 read on detecting the level of different thrombospondin fragments to diagnose cancer.

Inventions 1-37 and Inventions 75-111, 223-259 and 297-333 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the

instant case, the thrombospondin fragments of Inventions 1-37 can be used in the methods (Inventions 223-259) of detecting the level of different thrombospondin fragments to diagnose cancer, as well used in the methods (Inventions 75-111) of making antibodies specific to each fragment. Also in the methods of Inventions 297-333 for implementing an immunoassay to distinguish properly and improperly collected plasma samples.

14. Because these inventions are independent or distinct for the reasons given above and have acquired a separate status in the art in view of their different classification, restriction for examination purposes as indicated is proper.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571) 272-0831. The Examiner works a flexible schedule, however she can normally be reached between the hours of 7:30 am to 6:30 pm, with alternate Fridays off.

If attempts to reach the Examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
15 February 2007